

## **REMARKS**

### **I. Introduction**

This paper is submitted in response to the Office Action mailed June 1, 2006 for the above-identified patent application. Claims 1-14 are pending. Claim 11 has been withdrawn from consideration. Claims 1-10, 12 and 13 have been rejected. Claim 14 has been objected to.

### **II. Claim Objections**

The Examiner has objected to claim 14 as dependent upon a rejected base claim, but stated that claim 14 would be allowable if rewritten in independent form including the limitations of the base claim.

Applicants have amended claim 14 to include the limitations of independent claim 1. Thus, as amended, independent claim 14 is now in a condition for allowance.

### **III. The Rejections under 35 U.S.C. 112, second paragraph**

The Examiner has rejected claims 2-4 and 9-10 as indefinite under 35 U.S.C. 112, second paragraph, because he alleges there is insufficient basis for the limitation “the selective” in each of the claims. Applicants have amended claims 2-4 and 9-10 to delete this phrase and overcome the rejection.

The Examiner has also rejected claim 10 as indefinite under 35 U.S.C. 112, second paragraph. The Examiner states that the recitation of “a dual norepinephrine serotonin reuptake inhibitor (NSRI)” in independent claim 1 is interpreted to comprise only one NSRI and, therefore, claim 10 lacks antecedent basis for the limitation of “at least two of milnacipran, sibutramine, and an aminocyclopropane derivative.”

However, Applicants respectfully submit that the articles ‘a’ or ‘an’ as used in patent claims carries the meaning of ‘one or more.’ *KCJ Corp. v. Kinetics Concepts, Inc.*, 223 F.3d 1351, 1356 (Fed. Cir. 2000); *Tate Access Floors Inc. v. Interface Architectural Res.*, 279 F.3d 1357 (Fed. Cir. 2002). Accordingly, the recitation of “a dual norepinephrine serotonin reuptake inhibitor (NSRI)” in independent claim 1 should be properly construed as ‘one or more’ dual norepinephrine serotonin reuptake inhibitor (NSRI) or triple reuptake inhibitor (TRI). Accordingly, dependent claim 10 does not lack

antecedent basis for the limitation of “at least two of milnacipran, sibutramine, and an aminocyclopropane.”

**IV. Rejections under 35 U.S.C. § 103**

Claims 1-7 and 12-13 have been rejected under 35 U.S.C. 103(a) as obvious over U.S. Patent No. 4,478,836 to Mouzin *et al.* (“Mouzin”) in view of Moret *et al.* NEUROPHARMACOLOGY, 24:12, 1211-19 (1985) (“Moret”) and Ruoff, J. FAMILY PRACTICE, 43:6, S25-S34 (1996) (“Ruoff”).

The Examiner states that Mouzin and Moret disclose that milnacipran is a dual norepinephrine (NE) serotonin (5-HT) reuptake inhibitor that may be used to treat depression. The Examiner further states that Ruoff discloses that “treatment in the patient with chronic pain is no different than in patients without pain.” Moreover, that the antidepressant venlafaxine exerts antidepressant activity through selective inhibition of norepinephrine and serotonin uptake. Thus, the Examiner alleges that, once depression is diagnosed, it would be obvious for a person skilled in the art to use the claimed compounds to treat depression secondary to pain.

To establish obviousness, however, there must be some suggestion or motivation to modify the references or to combine the teachings. *See In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991); MPEP 2144.08(II)A. The disclosure of Ruoff would clearly lead a person of ordinary skill in the art away from using a norepinephrine serotonin reuptake inhibitor (NSRI) or triple reuptake inhibitor (TRI), as recited in the present invention. Ruoff discloses that a selective serotonin reuptake inhibitor (SSRI), such as fluoxetine, sertraline and paroxetine, are considered the *first-line treatment* for depression because of the demonstrated efficacy and well tolerated side-effect profile. *See* Ruoff page S28. Moreover, treatment of atypical depression with a MAO-I has been shown to be even more effective than with a SSRI. *See* McGrath *et al.*, *Am J Psychiatry* 2000;157(3):344-350 (copy attached). In contrast, therapy with an NSRI, such as venlafaxine, is disclosed to be associated with serious side-effects including nausea, vomiting, blood pressure, increase, sexual dysfunction, sweating and somnolence. *See* Ruoff page S30. In fact, Ruoff discloses that, due to its side effect profile, the NSRI venlafaxine should be reserved for use in the treatment of refractory depression. *See* Ruoff page S30. Thus,

Ruoff not only fails to teach the desirability of the claimed method, but in fact teaches away from using an NSRI or TRI, as claimed in the present invention. Consequently, Ruoff would not provide any motivation to administer a dual norepinephrine serotonin reuptake inhibitor (NSRI) or triple reuptake inhibitor (TRI) to alleviate or prevent at least one symptom of atypical depression, as recited in the present invention. Thus, reconsideration and withdrawal of the rejection of claims 1-7 and 12-13, as obvious over Mouzin in view of Moret and Ruoff, is respectfully requested.

Claim 8 has been rejected under 35 U.S.C. 103(a) as obvious over Mouzin in view of Moret and Ruoff, further in view of Shuto *et al*, J. MED. CHEM., 38 2964-68 (1995) ("Shuto"). For the reasons stated above, independent claim 1 is not obvious over Mouzin in view of Moret and Ruoff. The addition of Shuto also does not establish obviousness with respect to independent claim 1. Accordingly, dependent claim 8 is believed to be patentable for at least the same reasons.

Claim 9 has been rejected under 35 U.S.C. 103(a) as obvious over Mouzin in view of Moret and Ruoff, further in view of Puech *et al.*, INTER. CLINICAL PSYCHOPHARMACOLOGY, 12, 99-108 (1997) ("Puech"). For the reasons stated above, independent claim 1 is not obvious over Mouzin in view of Moret and Ruoff. The addition of Puech also does not establish obviousness with respect to independent claim 1. Accordingly, dependent claim 9 is believed to be patentable for at least the same reasons.

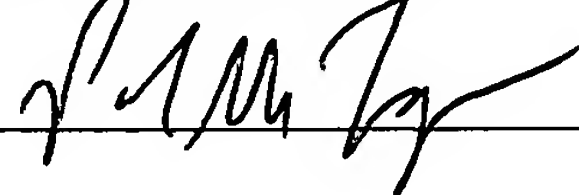
**V. Conclusion**

In view of the foregoing remarks, reconsideration and allowance of claims 1-10 and 12-14 is respectfully requested.

Applicants believe that the claims are now in a condition for allowance. However, if the Examiner believes that any outstanding issues could be resolved by an interview, the Examiner is asked to contact the undersigned below.

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Respectfully submitted,

By 

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